Cutaneous and Subcutaneous Blood Flow in Nonlesional Skin of Patients with Minimal Psoriatic Skin Manifestations

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Cutaneous and subcutaneous blood flow (CBF, SBF) were studied in nonlesional psoriatic skin (NLS) of 10 patients with only minimal psoriatic skin manifestations, using the local ^{133}Xe washout method. Measurements of the CBF and SBF in the NLS of the patients and 10 normal individuals yielded no statistically significant differences. The results of the present study indicate that the activity of psoriasis can be monitored by the CBF measurements in the NLS, since previously published values for CBF of NLS have shown increasing values with increasing psoriatic activity. The significance of these findings may be more evidence of humoral factors playing a role in the pathogenesis of the disease.

The tissue-to-blood partition coefficient for ^{133}Xe was calculated on the basis of biochemical estimations of the relative content of lipids, proteins, and water in skin biopsies from nonlesional skin sites of 8 psoriatic patients. The relative content of lipids, proteins, and water was normal. Thus, the normal ^{133}Xe partition coefficient of 0.7 ml/g should be used for measurements of the CBF in NLS. *J Invest Dermatol 86:582–584, 1986*

Nonlesional skin (NLS) of psoriatics is abnormal. Previous reports have demonstrated an increased metabolic or epidermal cell proliferation rate in the NLS [1]. Abnormal papillary capillaries might be found in recently healed skin [2,3] long after clinical resolution and in "never involved" skin [4–7]. The increased epidermal proliferation rate might not occur without an adequate vascular support. Recently, we reported that cutaneous blood flow (CBF) in NLS was high in patients with active [8,9] and chronic [10] psoriasis and that a decrease occurred during a 4-week treatment period [9], although the normal CBF levels were not reached. In 2 studies we found increased subcutaneous blood flow (SBF) in NLS areas [11,12].

In this study we report the CBF and SBF in psoriatic patients with only minimal psoriatic skin involvement.

MATERIALS AND METHODS

Patients and Controls Ten patients with well-established diagnosis of psoriasis vulgaris were selected for the study and these are shown in Table I. All patients had only minimal psoriatic skin involvement of the chronic, stable type at the time of measurement. No efforts were made to distinguish between NLS with previous psoriatic involvement or "never involved" NLS since photographic documentation proved that the memory of some of the patients was not always correct. None of the patients had active psoriasis at least 1 year prior to the measurement.

Ten normal individuals matched for age and sex served as controls, and these are also shown in Table I.

Measurements of CBF and SBF The ^{133}Xe washout method was used, and the same experimental procedure as recently described [10] was followed. All measurements were performed with a CdTe(Cl) minidetector attached to the skin surface on the proximal extensor site of the forearm, while the individuals were in the supine position. Room temperature was kept constant during the experiments at 21–22°C.

In order to quantitate the blood flow using the local ^{133}Xe washout method, it is necessary to know the tissue-to-blood partition coefficient for ^{133}Xe. In a previous study we found that the relative lipid content of lesional psoriatic skin was 2.5% compared with the normal 1%, and had an inverse ratio of the water and protein content [8]. These deviations significantly influenced the ^{133}Xe partition coefficient of lesional psoriatic skin [8]. Deviations from the normal content of lipids and proteins in NLS may also be due to the abnormal biochemical compositions of lipids in NLS that have been described earlier [13–16]. Previously reported changes in the blood flow rates for NLS may, therefore, be solely due to differences in the tissue-to-blood partition coefficient for ^{133}Xe [8]. It was therefore necessary to determine the relative lipid, water, and protein content in NLS of psoriatics in order to calculate a partition coefficient for ^{133}Xe in NLS.

Measurements of Water, Lipid, and Protein Content in Nonlesional Skin of Psoriatic Patients Sixteen biopsies from 8 patients with psoriasis vulgaris were selected for study after informed consent was obtained. Age and sex of the patients are shown in Table II. Two 4-mm punch biopsies were taken from NLS on the proximal, dorsal extensor site of the forearm after a ring of anesthesia 5–6 cm wide and at least 2 cm from the biopsy site was produced by intradermal injection of 1% lidocaine without epinephrine. Any subcutaneous tissue was carefully removed by dissection from the biopsies before both biopsies were placed in an air-tight glass tube and the weight of the biopsy material was calculated. Using this technique we have previously shown that the subcutaneous adipose tissue was not included in the biopsy and that the deep dermis was present in the samples [8]. After evaporation to total dryness and constant weight, the lipid

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Abbreviations:
CBF: cutaneous blood flow
NLS: nonlesional psoriatic skin
SBF: subcutaneous blood flow

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Table I. Cutaneous and Subcutaneous Blood Flow (CBF, SBF) in Patients with Minimal Psoriatic Skin Involvement Compared with Normal Individuals

Patient	Sex	Age	Psoriatic Skin Involvement (%)	CBF	SBF	Controls	Sex	Age	CBF	SBF
1	F	30	< 3	5.3 (0.7)	1.65 (0.02)	A	F	31	7.9 (0.1)	1.85 (0.08)
2	F	19	< 3	6.8 (0.04)	1.70 (0.15)	B	F	19	7.2 (0.1)	1.70 (0.01)
3	M	48	~ 1	6.5 (0.1)	2.65 (0.15)	C	M	49	5.9 (0.2)	2.08 (0.02)
4	F	20	< 3	7.1 (0.1)	1.65 (0.05)	D	F	19	7.0 (0.1)	3.40 (0.04)
5	F	59	< 3	7.1 (0.2)	1.55 (0.05)	E	F	60	6.2 (0.1)	0.55 (0.03)
6	F	50	<< 1	8.5 (0.2)	1.90 (0.05)	F	F	50	8.8 (0.2)	2.00 (0.55)
7	M	59	<< 1	5.5 (0.3)	1.05 (0.10)	G	M	58	8.1 (0.2)	2.38 (0.05)
8	F	61	<< 1	7.3 (0.1)	0.55 (0.05)	H	F	61	5.0 (0.2)	1.00 (0.04)
9	F	28	<< 1	6.7 (0.1)	3.20 (0.10)	I	F	28	9.0 (0.4)	1.85 (0.05)
10	M	56	< 1	8.5 (0.1)	1.75 (0.15)	J	M	53	9.1 (0.1)	2.40 (0.05)
Mean		43		6.9	1.77			43	7.4	1.92
±1 SD				0.8	0.53				1.0	0.56

One SD is shown within parentheses. Blood flow in ml · (100 g · min)$^{-1}$. Mean ± 95% confidence limits.

was extracted by: (1) chloroform:methanol (2:1, v/v); (2) chloroform : methanol (1:2), repeated twice; (3) chloroform:methanol (1:2) in a warm water bath for 30 min at 60°C; (4) chloroform:methanol (1:2) overnight; and finally (5) chloroform. The lipid extraction procedure was repeated twice, thereby removing all lipids from the tissue biopsies [17]. Following, the tissue was again evaporated to total dryness and weighed. The dry matter after extraction of water and lipids consists almost exclusively of proteins and very small quantities of minerals and carbohydrates. Minerals and carbohydrates do not contribute to the solubility coefficient. The dry matter is, therefore, for practical purposes, called "proteins."

Calculations of the Partition Coefficient for ^{133}Xe in NLS of Psoriatics Knowing the relative content of water, proteins, and lipids in the NLS, the solubility of ^{133}Xe was calculated as described by Yeh and Petterson [18]. The solubility of ^{133}Xe in blood was previously calculated to 148.5 ml/100 g at 37°C [8]. The partition coefficient was then calculated by dividing the solubility coefficient of ^{133}Xe in NLS of psoriatics by the solubility of ^{133}Xe in blood.

For subcutaneous tissue in the psoriatics and the normal individuals, a partition coefficient of 5 ml/g was used [11].

Statistics The Wilcoxon test for unpaired samples was used to analyze the results. A 95% confidence limit for the means was calculated using the Student's *t*-distribution.

RESULTS

Using the relative content of water, lipid, and proteins in the skin biopsies from NLS that are summarized in Table II, the tissue-to-blood partition coefficient for ^{133}Xe in NLS was calculated as being 0.8 ml/g.

Using the values for normal skin, i.e., 72.5% water, 1% lipid, and 26.5% proteins [19], the tissue-to-blood partition coefficient for ^{133}Xe in normal skin is also calculated as being 0.8 ml/g.

For reasons explained later, a partition coefficient of 0.7 ml/g was used for both NLS and skin of normal individuals. CBF and SBF measurements in the psoriatics and the normal individuals are shown in Table I. There was no statistically significant difference between the blood flow values obtained.

Table II. Relative Content of Water, Lipid, and Proteins in Nonlesional Skin of Patients with Psoriasis

Patients	Sex	Age	Water (%)	Lipid (%)	Protein (%)
1	F	38	70.2	1.8	28.0
2	F	31	71.6	1.0	27.4
3	M	48	74.4	2.9	22.7
4	F	31	74.6	0.6	24.8
5	F	67	79.1	0.3	20.6
6	M	51	69.4	2.7	27.9
7	M	33	69.8	0.2	30.0
8	F	66	72.4	1.2	26.4
Mean		46	72.7	1.3	26.0
±1 SD		15	3.3	1.0	3.1

DISCUSSION

In this study we found a normal relative content of lipid, water, and proteins in NLS of psoriatics. Calculations of the tissue-to-blood partition coefficient for ^{133}Xe in NLS gave a value of 0.8 ml/g, which is identical to that of normal individuals. The same value was calculated by Sejrsen [20]. The solubility of ^{133}Xe is dependent on the temperature. Since the skin temperature is probably lower than 37°C the calculated partition coefficient might be slightly overestimated. It has, therefore, often been considered practical to use the value of 0.7 ml/g for both normal cutaneous tissue and other "low-lipid" tissues (e.g., muscles). This tradition was followed in this study.

Enhanced metabolic and proliferative activity of the epidermis of NLS has been demonstrated by a variety of techniques—as reviewed by Krueger [1]—and show mean values about 1.5 times higher than measurements in normal individuals. However, values obtained in NLS and skin in normal individuals overlap. This disparity—some patients with elevated epidermal metabolic activity in the NLS and others with normal levels—might be due to differences in the clinical state of the psoriasis, i.e., active or chronic lesions and the percentage of the lesional skin surface involvement.

We have previously proposed that the elevated SBF in psoriatics might be explained as being due to either an extracutaneous psoriatic manifestation of the disease or as a secondary, thermoregulatory phenomenon due to an increased heat loss in the skin (the increased heat loss should then be due to the elevated CBF [11]). The results of the SBF measurements in the present study are, however, in accordance with both of these explanations.

The results of the present and previous studies show that CBF and SBF in both lesional and NLS and the severity of psoriasis seem to be directly related [8–11].

CBF in NLS of psoriatics with active psoriasis was twice as high as normal CBF. During a 4-week treatment period the CBF of NLS decreased to 1.8 times the normal CBF. In patients with the chronic stable type of psoriasis, CBF of NLS was 1.4 times higher than normal CBF. Thus, the local ^{133}Xe washout method

is so far the only method that has proved useful in distinguishing abnormalities in the psoriatic NLS. It is, however, unclear why the CBF of NLS is elevated with increasing psoriatic activity. The results may be interpreted as more indirect evidence of humoral factors governing the expression of the disease on a total-body basis at any given time—as was proposed earlier by Krueger [1].

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